

**Notice of Allowability**

Application No.

10/081,974

Examiner

Traviss C. McIntosh

Applicant(s)

RUBINFELD ET AL.

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**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to amendment filed 4/19/2005.
2. ☒ The allowed claim(s) is/are 1,13-16,18-21 and 25.
3. ☐ The drawings filed on \_\_\_\_\_ are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
    1. ☐ Certified copies of the priority documents have been received.
    2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
  - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
    - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
  - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08),  
Paper No./Mail Date \_\_\_\_\_
4. ☐ Examiner's Comment Regarding Requirement for Deposit  
of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413),  
Paper No./Mail Date \_\_\_\_\_
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_\_

JAMES O. WILSON  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600

### EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Shirley Chen on June 20, 2005.

The application has been amended as follows:

Claim 1 (currently amended): A method for treating cancer in a patient, wherein the cancer has a p53 mutation, comprising:

administering 5-fluorouracil to said patient; and

administering to said patient 9-nitro-20(S)-camptothecin or 9-amino-20(S)-camptothecin at least 1 day after administering 5-fluorouracil to the patient and when 5-fluorouracil is not present in a pharmaceutically active form in said patient.

Claim 21 (currently amended): A method according to claim 1 wherein said patient has pancreatic cancer.

Claim 25 (currently amended): A method according to claim 1 wherein said patient has cancer selected from the group consisting of acute myelogenous leukemia, cholangiocarcinoma,

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chronic myelogenous leukemia, lymphoma, melanoma, multiple myeloma, osteosarcoma, gastric sarcoma, glioma, bladder, breast, cervical, colorectal, lung, ovarian, pancreatic, prostate, and stomach cancer.

The following is an examiner's statement of reasons for allowance: the closest prior art is seen to be Bernacki et al., Rubinfeld, and Achterrath, and none of the references are seen to teach or fairly suggest the specific sequential therapy recited in claim 1, i.e., administration of 5FU at least 24 hrs before administration of 9NC or 9AC. In contrast, Bernacki et al. discloses in vitro studies of the combination of 9NC and 5FU concurrently or with 5FU administered after 9NC. In particular, Bernacki et al. found that "sequential combination of 9NC or SN-38 followed by 5-FU, 24 hr later appeared to be highly synergistic at high dose-effect levels (i.e., ID<sub>90</sub>), suggesting that sequential drug administration may be more efficacious at high effect level and that the order of drug addition is very important." (see abstract). In view of this teaching of the importance of the order of administration and the synergistic effects of sequential combination of 9NC followed by 5-FU, one of ordinary skill in the art would not be motivated to reverse the order of administration of 9NC and 5-FU to arrive at the claimed invention. Also, none of the cited references teaches or fairly suggests administering 9NC (or 9AC) at least 1 day after administration of 5FU in a patient with cancer cells having a p53 mutation. Rubinfeld neither teaches administering 9NC or 9AC to a cancer patient at least 1 day before or after administration of 5-FU. Additionally, Achterrath fails to teach the claimed sequential therapy as Achterrath teaches a combination therapy of a water soluble 5-camptothecin derivative CPT-11,

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5-FU, and folinic acid and wherein the administration of the combination of agents is administered within a 24 hour time period (see column 5, lines 23-28).

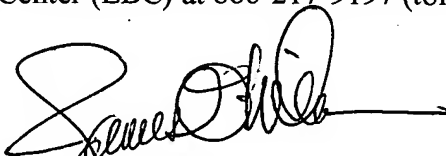
Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C. McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Traviss C. McIntosh III  
June 20, 2005



James O. Wilson  
Supervisory Patent Examiner  
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